SafetyCall International, PLLC

Recalls: Trends, Management, Opportunity and Challenges?

Rick Kingston, PharmD
President, Regulatory and Scientific Affairs & Sr. Clinical Toxicologist
SafetyCall International, P.L.L.C.
Adverse Event Call Center
&
Clinical Professor of Pharmacy
College of Pharmacy, University of Minnesota
Call Transfer Procedures

Topics for Today's Presentation

- Recalls: Are increasing recalls indicating decreasing product quality and safety?
- What is giving rise to the numbers?
- Issues "potentially" contributing to the rise to recalls
- Impact of consumer perceptions of risk and safety
- HHE's: Step-by-Step evaluation of safety risks impacting appropriate recall categorization
- Conclusions and Key Take-Home Points

FDA-regulated Products Subject to Recall

- Human drugs
- Animal drugs
- Medical devices
- Radiation-emitting products
- Vaccines
- Blood and blood products
- Transplantable human tissue
- Animal feed
- Cosmetics
- About 80 percent of the foods eaten in the United States

Recall Classifications

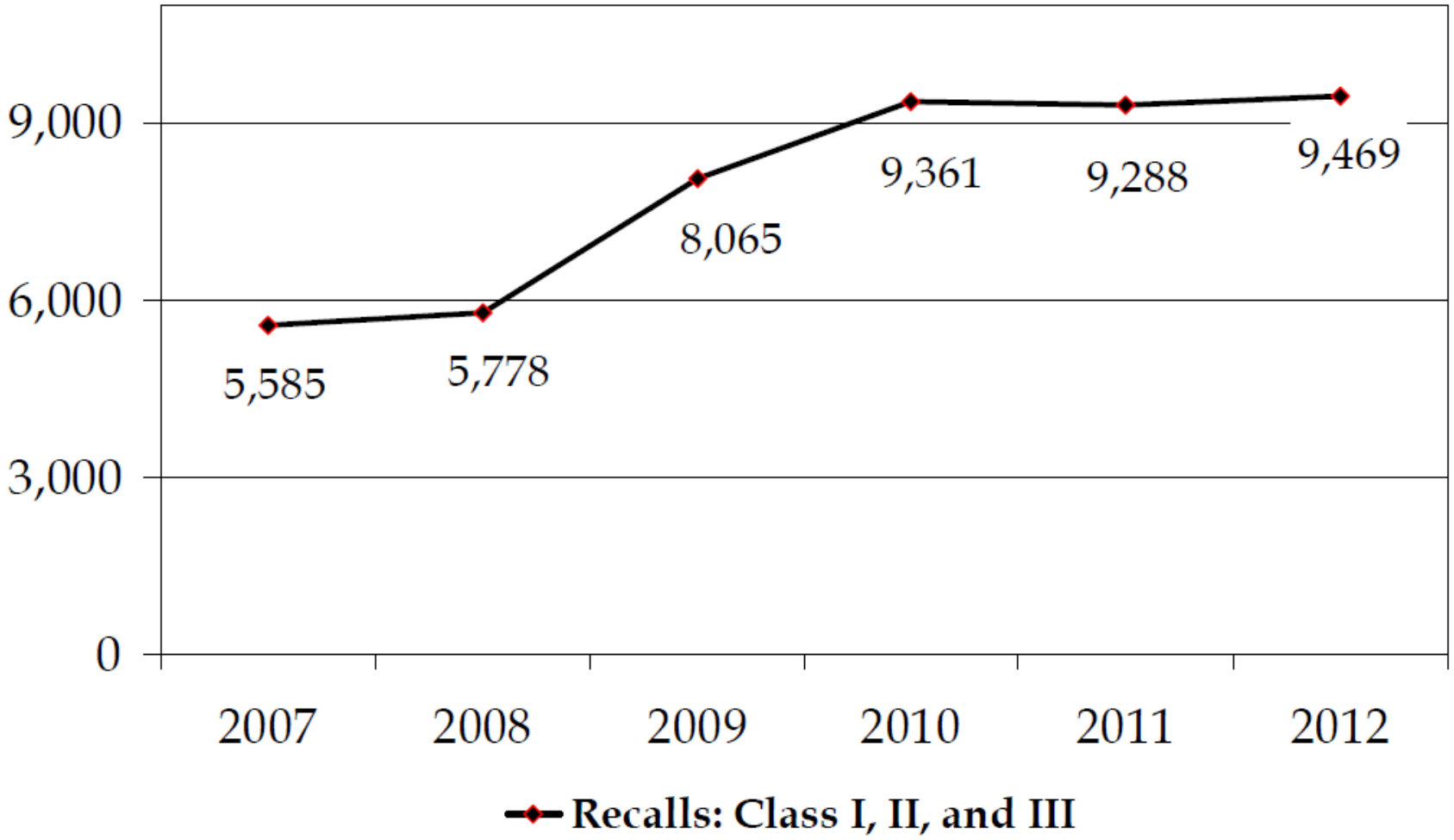
These guidelines categorize all recalls into one of three classes, according to the level of hazard involved:

- **Class I:** Dangerous or defective products that predictably could cause serious health problems or death. Examples include: food found to contain botulinum toxin, food with undeclared allergens, a label mix-up on a lifesaving drug, or a defective artificial heart valve.
- **Class II:** Products that might cause a temporary health problem, or pose only a slight threat of a serious nature. Example: a drug that is under-strength but that is not used to treat life-threatening situations.
- **Class III:** Products that are unlikely to cause any adverse health reaction, but that violate FDA labeling or manufacturing laws. Examples include: a minor container defect and lack of English labeling in retail food.

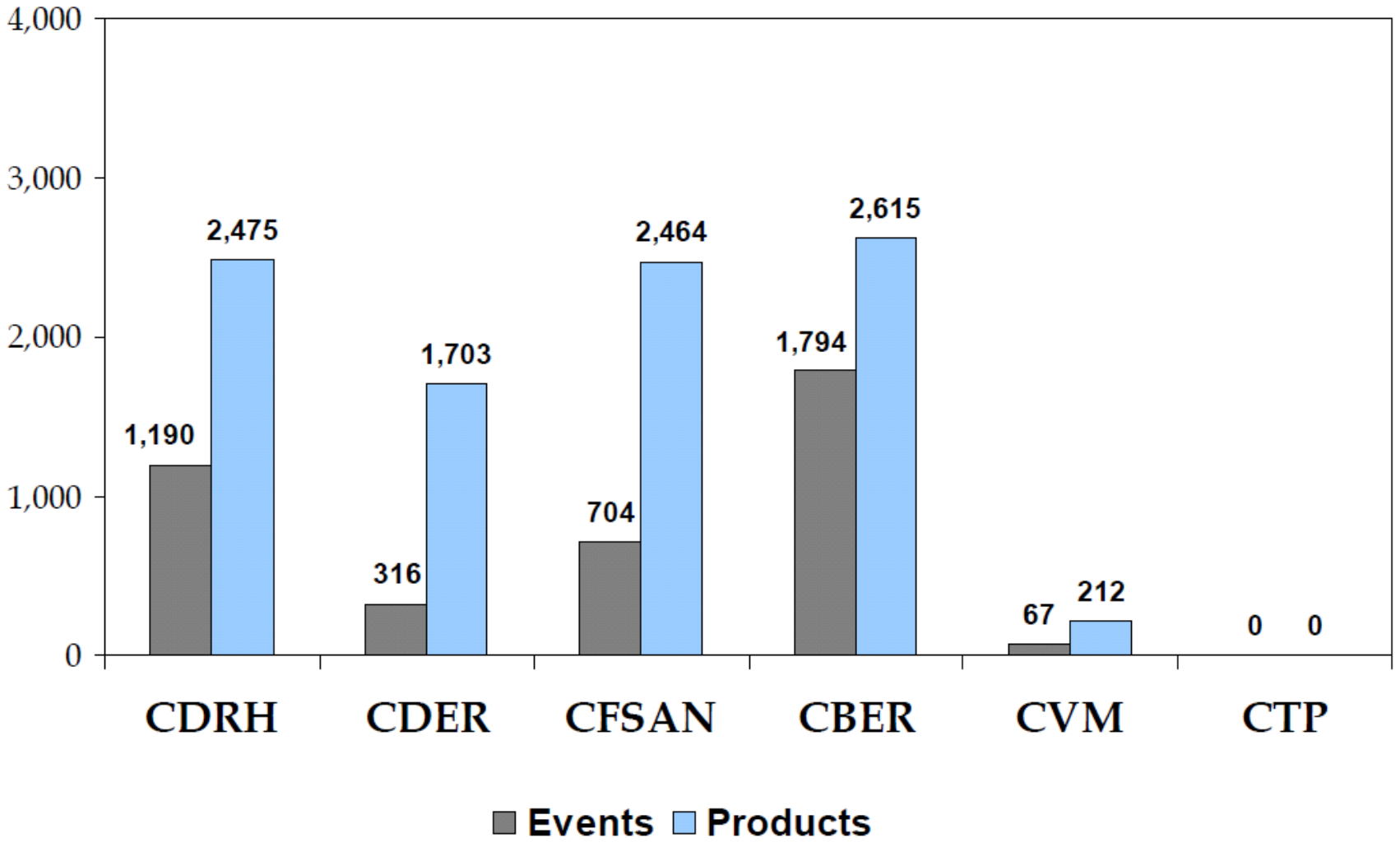
FDA Enforcement Statistics Summary Fiscal Year 2012

Seizures	**8**
Injunctions	**17**
Warning Letters	**4,882**
Recall Events	**4,075**
Recalled Products	**9,469**
Debarments	**20**

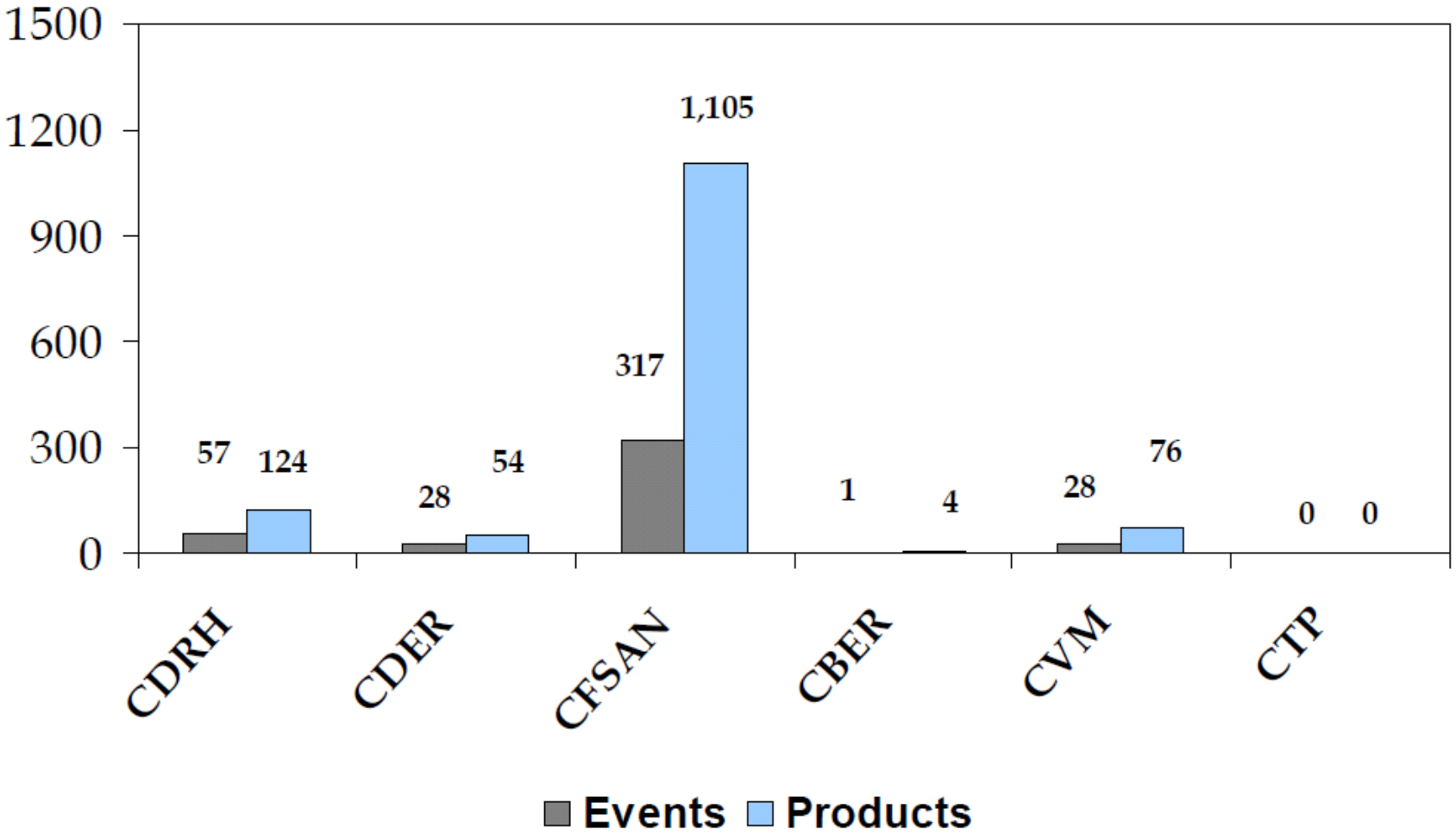
Recalled Products – All Centers
Fiscal Years 2007 – 2012



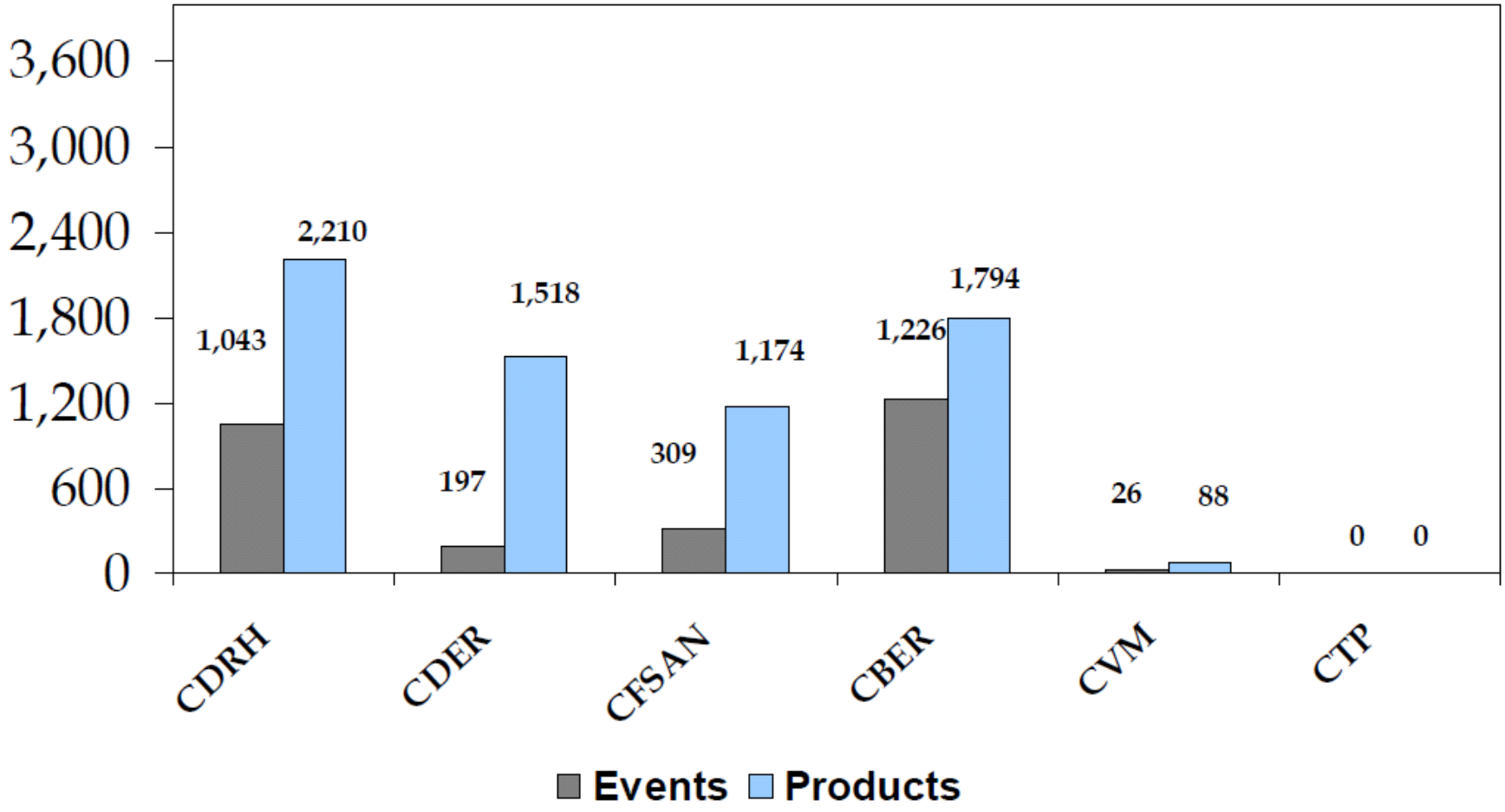
FDA Recalls By Center - All Classes
Fiscal Year 2012



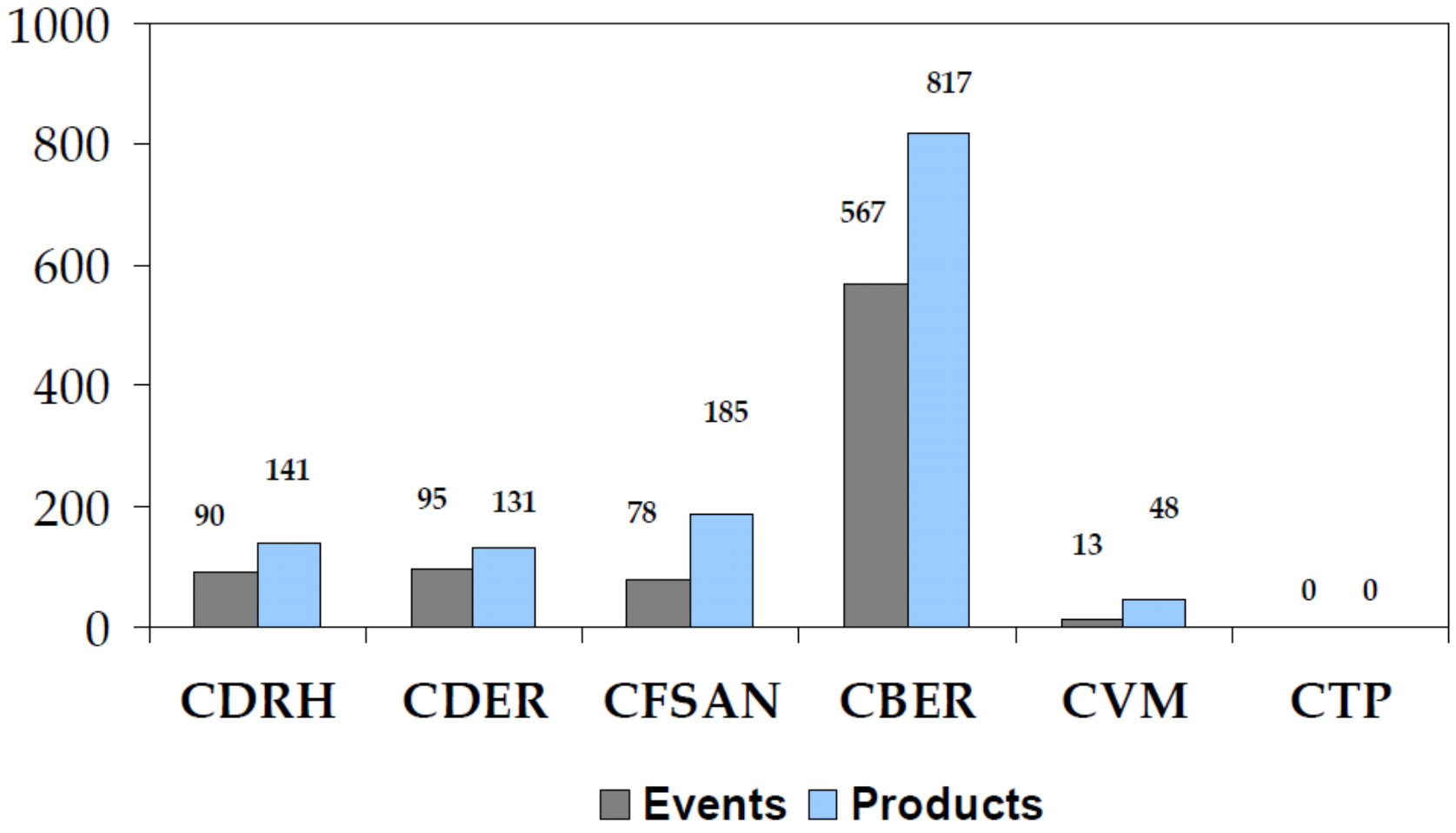
FDA Recalls – Class I By Center
Fiscal Year 2012



FDA Recalls - Class II By Center
Fiscal Year 2012



FDA Recalls - Class III By Center Fiscal Year 2012



RESEARCH LETTER

ONLINE FIRST | HEALTH CARE REFORM

The Frequency and Characteristics of Dietary Supplement Recalls in the United States

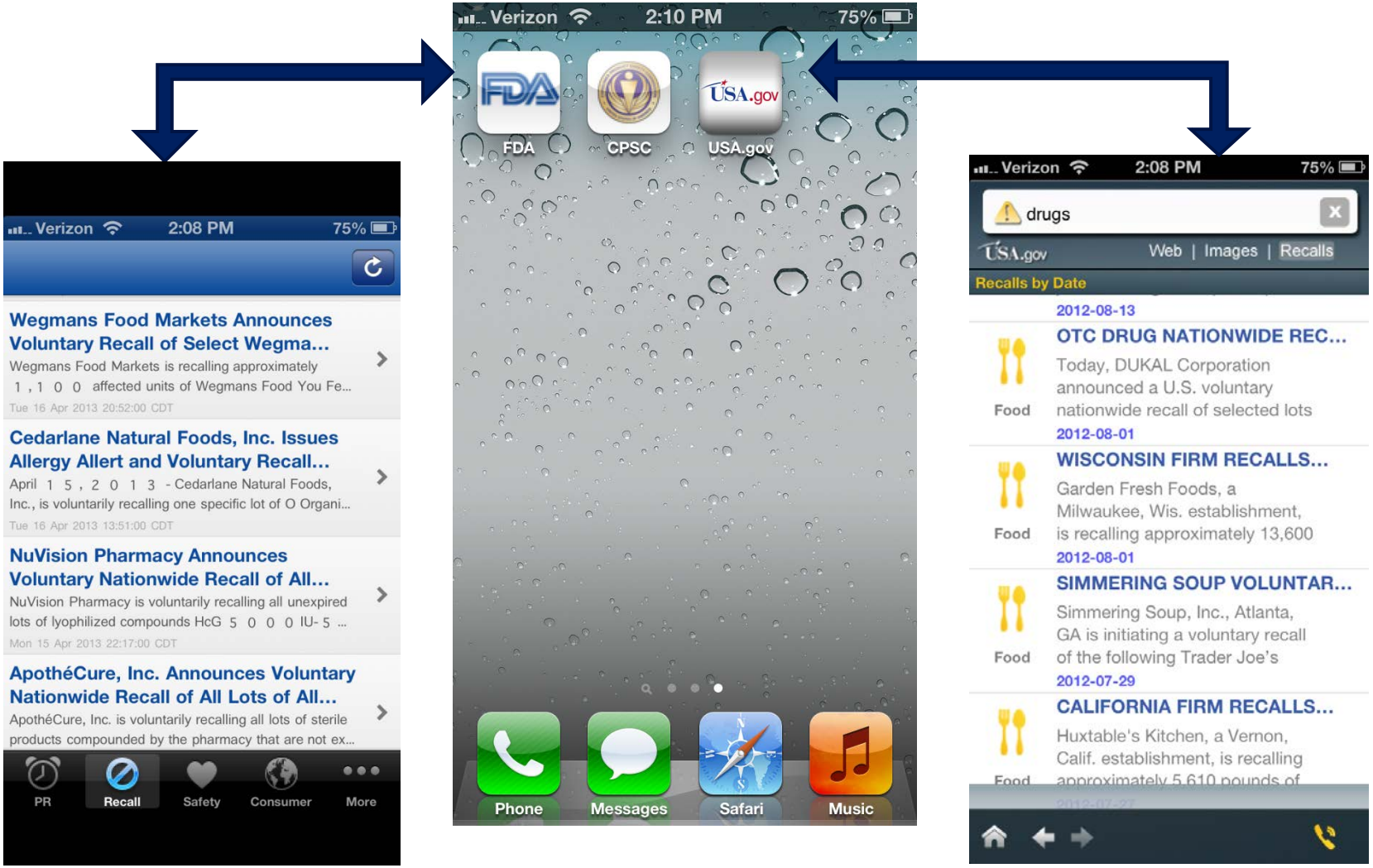
Results. From January 1, 2004, through December 19, 2012, 465 drugs were subject to a class I recall in the United States. Just over one-half (237 [51%]) were classified as dietary supplements as opposed to pharmaceutical products (**Table**). Most recalls occurred after 2008 (210 [89%]). Supplements marketed as sexual enhancement products (95 [40%]) were the most commonly recalled dietary supplement product, followed by bodybuilding (73 [31%]) and weight loss products (64 [27%]). Unapproved drug ingredients (237) accounted for all recalls. Fifty-seven recalled products (24%) were manufactured outside of the United States. There were 147 recalls (62%) that involved units distributed internationally.

Table. Characteristics of Class I Drug Recalls of Dietary Supplements, 2004 to 2012

Characteristic	Supplements, No. (%)
Drug products recalled, Total No.	237 (100)
Recalls by year, No.	
2012	16 (7)
2011	30 (13)
2010	117 (49)
2009	47 (20)
2008	8 (3)
2007	12 (5)
2006	0
2005	5 (2)
2004	2 (1)
Type of dietary supplement	
Weight loss	64 (27)
Bodybuilding	73 (31)
Sexual enhancement	95 (40)
Other	5 (2)
Manufacturing region	
United States	175 (74)
Outside the United States	57 (24)
Not recorded	5 (2)
Reason for recall	
Unapproved ingredient/unapproved drug	237 (100)
Lots recalled	
1	17 (7)
2-25	14 (6)
>25 or all	161 (68)
Data not available	45 (19)
Extent of distribution	
Several states	8 (3)
Nationwide and Puerto Rico	82 (35)
Beyond the United States and Puerto Rico	147 (62)
Recalls with adverse events mentioned in FDA Enforcement Reports	0

Why are Recalls on the Increase?

1. Analytical/Technological advances
2. Advances in science and research
3. Increased regulatory compliance audits
4. Mandatory AER reporting
5. Corporate expectations of quality and concern over citations
6. Investor expectations of quality and concern over citations
7. Liability concerns: those that knew, those that didn't and those that should have
8. Globalization, increased complexity of the supply chain, traceability
9. Publicity: discovery, disclosure, media hype, and info sharing
10. Consumer (mis)perceptions of risk, safety and expectations of quality


Verizon 2:08 PM 75%
Wegmans Food Markets Announces Voluntary Recall of Select Wegma...
Wegmans Food Markets is recalling approximately 1,100 affected units of Wegmans Food You Fe...
Tue 16 Apr 2013 20:52:00 CDT
Cedarlane Natural Foods, Inc. Issues Allergy Allert and Voluntary Recall...
April 15, 2013 - Cedarlane Natural Foods, Inc., is voluntarily recalling one specific lot of O Organi...
Tue 16 Apr 2013 13:51:00 CDT
NuVision Pharmacy Announces Voluntary Nationwide Recall of All...
NuVision Pharmacy is voluntarily recalling all unexpired lots of lyophilized compounds HcG 5000 IU- 5 ...
Mon 15 Apr 2013 22:17:00 CDT
ApothéCure, Inc. Announces Voluntary Nationwide Recall of All Lots of All...
ApothéCure, Inc. is voluntarily recalling all lots of sterile products compounded by the pharmacy that are not ex...
PR
Recall
Safety
Consumer
More
Verizon 2:10 PM 75%
FDA
CPSC
USA.gov
Phone
Messages
Safari
Music
Verizon 2:08 PM 75%
drugs
USA.gov
Web | Images | Recalls
Recalls by Date
2012-08-13
OTC DRUG NATIONWIDE REC...
Today, DUKAL Corporation announced a U.S. voluntary nationwide recall of selected lots
Food
2012-08-01
WISCONSIN FIRM RECALLS...
Garden Fresh Foods, a Milwaukee, Wis. establishment, is recalling approximately 13,600
Food
2012-08-01
SIMMERING SOUP VOLUNTAR...
Simmering Soup, Inc., Atlanta, GA is initiating a voluntary recall of the following Trader Joe's
Food
2012-07-29
CALIFORNIA FIRM RECALLS...
Huxtable's Kitchen, a Vernon, Calif. establishment, is recalling approximately 5,610 pounds of
Food

You may be facing a recall if:

- NTP (National Toxicology Program) labels your health promoting active ingredient a known carcinogen
- Your Chinese supplier was raided by authorities and…
- Rachael Ray's dog has been poisoned and your product was the last thing in its mouth
- Consumer Reports found…
- Dr. Oz says…

http://www.youtube.com/watch?v=zEDE9BFaV_g

Post-Market Surveillance Impact on Recalls

Goals of Post-Market Surveillance

- Helps identify intended ***and*** unintended use patterns that may potentially contribute to "unintended effects"
- Allows assessment of how the product performs by itself or in the presence of other products or substances
- Creates an opportunity for identifying or investigating imminent safety risks:
  - Aids in determining the need for mitigation, level of mitigation and likely success of various options for mitigation

Tip of the Iceberg Phenomena

Study Population Size Necessary to Identify 1, 2, or 3 Cases of a Given Effect Based on its Relative Incidence

AE Frequency	Number of AE Cases		
	1	2	3
1 out of 100	300	480	650
1 out of 200	600	960	1,300
1 out of 1,000	3,000	4,800	6,500
1 out of 2,000	6,000	9,600	13,000
1 out of 10,000	30,000	48,000	65,000

Post-Market Surveillance Data Influencing Recall Decisions

1. Normalized Incidence Rates
2. Determining acceptable ranges and actionable variations
3. Determining expected events based on toxicology and product design
4. Identifying predictable events and their expected incidence rates

Post-Market Surveillance Data Influencing Recall Decisions

5. Incident integrity scoring (consider that most consumer health care product events are spontaneously reported vs. clinical trial generated)
6. Identifying "background noise" or events occurring simultaneously but unrelated to product use

   Also remember… not all AERs are due to background noise

7. Identifying trends in low scoring unexpected events and considering potential relationship to product issues i.e. "Sentinel Events"

Post-Market Surveillance Data Influencing Recall Decisions

8. For suspected “Sentinel” events or for deviations in expected incidence rates, do individual incidents represent a potential recall issue:
   a. Quality Control Issues/Contamination
      - Before leaving the plant
      - After leaving the plant
   b. Direct but predictable or previously recognized adverse effects based on inherent toxicology/pharmacology of the product or an ingredient
      - Dose dependent
      - Dose independent (idiosyncratic)

Post-Market Surveillance Data Influencing Recall Decisions

c. Direct but previously unrecognized adverse effect of the product or an ingredient:
   - Idiosyncratic, unpredictable in occurrence but predictably occurring at a low incidence rate with the population
   - Long term effects secondary to chronicity of use

d. Interaction related event involving use of the product and:
   - Other drug
   - Disease
   - Food
   - Environment
   - Biologic (gene expression)
   - Other consumer product concomitantly being used

e. Counterfeit Product

Post-Market Surveillance Data Influencing Recall Decisions

9. Are reported events in any given category preventable?
10. Can reported effects in any given category be prevented, managed and/or mitigated through:
    a. Disclosure
    b. Education
    c. Reformulation
    d. New manufacturing process (change in solvents)
    e. New product design (multi-ingredient review)
    f. Dosage adjustment
    g. Market withdrawal or recall

Health Hazard Evaluation (HHE)

- Health Hazard Evaluation Document: the primary stakeholder communication tool
  - Investigation details
  - Affected product summary
  - Expected or observed consumer experience related to the issue
  - Mitigation plans

Health Hazard Evaluation (HHE) Preliminary Investigation Details

- Identification of suspected issue
- Root cause analysis and status review
  - How did it happen
  - How much product affected
  - How much in quarantine
  - How much distributed and at what level
  - How much retrieved prior to distribution
  - How much unaccounted for

Health Hazard Evaluation (HHE) Affected Product Summary

- Product/Ingredient summary:
  - Description of the inherent pharmacology/toxicology the product/ingredients affected
  - Description of the toxicological/safety significance of the issue
  - Description of the exposure opportunity
  - Issue status in terms of consumer exposure (potential)

Health Hazard Evaluation (HHE)
Expected or Observed Consumer Experience

Questions to ask and answer:

1. Have there been any reports of illness or injury from the product?
2. Are there any existing conditions that might put an individual at further risk?
3. Are there individuals that would be at greater risk than others to develop adverse medical consequence to product use?

Health Hazard Evaluation (HHE)
Expected or Observed Consumer Experience

4. How serious of a health hazard is involved with the affected products?
5. How likely is it that any given consumer will experience an adverse consequence?
6. What is the long term consequence associated with any reported adverse effect?

Mitigation Options

- Recall (withdrawal) options:
  - Consumer level
  - Retail level
  - Distribution
  - Warehouse
  - Manufacturer level

Take Home Points

- Safety First!
  - Would you give the product to your 2 year old?
- Recall decisions must meet internal, external and regulatory needs
  - Not all “recalls” are created equal
- Post-market surveillance supports pre and post event decision making
- Prevention

SafetyCall International, PLLC

Thank you!

rkingston@safetycall.com

www.safetycall.com

twitter.com/safetycall